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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,882	03/02/2000	DUNCAN MCGREGOR	1015-00	3081

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 05/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,882	MCGREGOR, DUNCAN	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/13/03 has been entered.

2. The amendments filed on 5/29/03, 6/13/03 and 6/17/03, 6/26/03 have been fully considered and entered into the application. The amendment filed on 6/26/03 is a copy of amendment filed on 6/17/03. The amendment filed on 6/13/03 added new claims 11-12, which are renumbered as claims 24-25 according to Rule 126.

3. Claims 1, 3-10 and 24-25 are currently pending in this application.

Priority

4. This application is a 371 of PCT/GB98/02630, which claims priority to a UK Application 9718455.

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The references cited in the Information Disclosure Statements filed on 3/9/01 and 1/20/04 have been fully considered.

Specification

7. The substitute specification filed on 10/8/02 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: a statement that "the substituted specification includes no new matter" was missing.

Claim Rejections - 35 USC § 112

8. Claims 1-10, 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 24, 25 recite that the 'chimeric protein-encoding portion of the recombinant polynucleotide is protected by a binding moiety which is a protein..', which is vague and indefinite, because it is not clear does applicants mean that the recombinant polynucleotide which is not bound by the DNA binding proteins is linked to a protein or covered by a protein. It is not clear what does applicants mean by protected by.

Claim 6 is vague indefinite by reciting 'can be'.

Claim 24 is vague and indefinite by reciting 'at least the chimeric protein-encoding portion not bound by the binding moiety', it is not clear what does applicants mean by at least chimeric protein encoding portion, does applicants mean that chimeric protein encoding portion of the polynucleotide is alos bound by the nucleotide binding portion, and the portion of the chimeric protein encoding portion not bound by the nucleotide binding portion is protected by the coat protein. Does applicants mean that the chimeric protein encoding polynucleotide is bound to the coat protein or is it covered by the coat protein. Applicants are requested to clarify. Further, the claim is indefinite by reciting 'can be.'

Claim Rejections - 35 USC § 102 and 103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 3-6, 8-10 and 25 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 5,498,530 (Schatz et al).

The instant claims briefly recite a synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, wherein the chimeric protein has a) a nucleotide binding portion, which comprises a binding domain of a nuclear steroid receptor; and b) a target peptide portion, and said recombinant polynucleotide comprises a) a chimeric protein encoding portion which encodes the chimeric protein of the complex; and b) a nucleotide sequence motif which is specifically bound by the nucleotide binding portion of the chimeric protein, and the chimeric protein encoding portion of the polynucleotide is not bound by the chimeric protein, and is protected by a binding protein, which is able to bind non-specifically to polynucleotides.

NOTE the recitation 'for use as a peptide display carrier package' is considered as intended use, and Claim 10 limitations are considered as product-by-process limitations.

Schatz et al teach peptide libraries and screening. The reference teaches methods of generating peptide library, the method comprises a) constructing a recombinant DNA vector that encoded DNA binding protein and contains a binding site for the DNA binding protein (refers to the recombinant polynucleoitdes of the instant claims); and the vector encodes a fusion protein composed of DNA binding protein and the peptide (refers to the target) (chimeric protein of the instant claims). And the reference teaches that during the screening methods, the fusion proteins remain bound to the vector that encodes the fusion protein (refers to the instant claim recombinant polynucleotide and chimeric protein complex) (for example, see column 2). The reference teaches the use of different DNA binding proteins (for example, see column 6), which includes nuclear hormone receptor-type proteins, and the reference preferentially uses *lac* repressor as the DNA binding protein. At some point during the growth of the transformants, the fusion protein will be expressed, and because of the random peptide also contains DNA binding sites for DNA binding proteins, fusion proteins will bind to the vectors that encode them to form a complex (i.e., see column 11). The reference teaches that the DNA of the vector contain one or random peptide coding sequence and spacer (i.e., see column 8) (refers to instant claim 5). Further the reference teaches that the lac repressor fusion proteins of the present invention include not only carboxy terminus fusion but also amino terminus fusions (i.e., see column 7) (refers to instant claim 9).

The reference do not specifically teach the complex of chimeric protein comprising nuclear steroid receptor as DNA binding proteins. However, it would have been obvious to one

skilled in the art at the time the invention was made to use the steroid receptor domains as DNA binding portion of the instant claims, because Schatz et al teach the advantages of the use of DNA binding moieties in phage vector screening, and teaches that the nuclear hormone receptors proteins as DNA binding proteins. The claimed invention differs from the prior art teachings by reciting that the chimeric encoding portion of the recombinant polynucleotide is protected by a protein. Schatz et al teach recombinant polynucleotide and a chimeric protein complex. Schatz et al do not teach chimeric protein encoding portion of the polynucleotide is protected by a protein.

The claimed synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare whether the chimeric encoding portion of the polynucleotide is protected by a protein (which is coat protein of the phage). The reference teaches the use of bacteriophage as the vector, same as the instant invention, and further the reference complex has all the components of the invention, thus the reference vectors are considered same as the instant claim vectors, thus the chimeric protein encoding portion is considered as protected by coat protein. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed synthetic construct (vector) is different from the one taught by prior art and to establish the patentable differences. See in re Best 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and Ex parte Gray 10 USPQ2d 1922(PTO Bedpan. App. & Int. 1989).

12. Claims 1, 3-10 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,498,530 (Schatz et al) and US Patent 6,451,527 B1 (Larocca et al).

The instant claims briefly recite a synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, wherein the chimeric protein has a) a nucleotide binding portion, which comprises a binding domain of a nuclear steroid receptor; and b) a target peptide portion, and said recombinant polynucleotide comprises a) a chimeric protein encoding portion which encodes the chimeric protein of the complex; and b) a nucleotide sequence motif which is specifically bound by the nucleotide binding portion of the chimeric protein, and the chimeric protein encoding portion of the polynucleotide is not bound by the chimeric protein, and is protected by a binding protein, which is able to bind non-specifically to polynucleotides.

NOTE the recitation 'for use as a peptide display carrier package' is considered as intended use, and claim 10 is considered as product-by-process limitation.

Schatz et al teach peptide libraries and screening. The reference teaches methods of generating peptide library, the method comprises a) constructing a recombinant DNA vector that encoded DNA binding protein and contains a binding site for the DNA binding protein (refers to the recombinant polynucleoitdes of the instant claims); and the vector encodes a fusion protein composed of DNA binding protein and the peptide (refers to the target) (chimeric protein of the instant claims). And the reference teaches that during the screening methods, the fusion proteins remain bound to the vector that encodes the fusion protein (refers to the instant claim recombinant polynucleotide and chimeric protein complex) (for example, see column 2). The reference teaches the use of different DNA binding proteins (for example, see column 6), which includes nuclear hormone receptor-type proteins, and the reference preferentially uses *lac* repressor as the DNA binding protein. At some point during the growth of the transformants, the

fusion protein will be expressed, and because of the random peptide also contains DNA binding sites for DNA binding proteins, fusion proteins will bind to the vectors that encode them to form a complex (i.e., see column 11). The reference teaches that the DNA of the vector contain one or random peptide coding sequence and spacer (i.e., see column 8) (refers to instant claim 5). Further the reference teaches that the lac repressor fusion proteins of the present invention include not only carboxy terminus fusion but also amino terminus fusions (i.e., see column 7) (refers to instant claim 9).

The reference do not specifically teach the complex of chimeric protein comprising nuclear steroid receptor as DNA binding proteins, and reciting that the chimeric encoding portion of the recombinant polynucleotide is protected by a protein. Larocca et al teach genetic package display system for selecting internalized ligands. The reference teaches that in an alternative embodiment, recovery of replicated internalized nucleic acid molecules may be achieved via a nucleic acid binding domain. Accordingly, when using phage, the phage genome can be altered such that a DNA binding sequence is incorporated therein. The phage may contain one or more copies of lac operon (i.e., see column 14). The reference teaches that a variety of nucleic acid binding proteins can be used in the claimed method, because of their sequence specific recognition. Host transcription factors have been grouped into seven well-established classes based upon the structural motif used for recognition. The major families include helix-turn-helix (HLH) proteins, homeodomains, zinc finger proteins, steroid receptors, leucine zipper proteins, helix-loop-helix(HLH) proteins, and P-sheets (refers to the steroid receptor of the instant claims) (i.e., see column 14). The reference further teaches steroid receptor proteins include receptors for steroid hormones, retinoids, vitamin D, thyroid hormones as well as other compounds. Specific

examples include retinoic acid, knipprs, progesterone, androgen, glucosteroid and estrogen receptor proteins (i.e., see column 15). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use different steroid receptors as DNA binding proteins in phage vector systems, because Larocca et al and Schatz et al teach the advantages of the use of DNA binding proteins in screening the phage vectors. And a person skilled in the art would have been motivated to use the steroid receptor proteins as DNA binding proteins, because the methods provide peptides with free carboxy or amino terminus, and add diversity in the structure for receptor binding.

Response to Arguments

13. Applicant's arguments with respect to claims 1-10 (rejections under 35 USC. 112, second paragraph) have been considered but are moot in view of the new ground(s) of rejection and amendments to the claims.

14. Applicant's arguments with respect to art rejection of claims 1-10, have been considered but are moot in view of the new ground(s) of rejection. Applicants arguments that Schatz et al does no refer to a DNA binding portion being a binding domain of a nuclear steroid receptor, as is required in claim 1 as amended, have been considered and are not persuasive. Because Schatz et al teach the various different types of DNA binding proteins, and exemplifies that nuclear hormone receptors can be used DNA binding proteins (i.e., see column 6). And applicants arguments regarding 'binding moiety' has been considered and is not persuasive, since the instant claim vectors and the reference vectors are same, it would have been obvious that the DNA which is not bound by the DNA binding protein is bound to the coat protein. Thus, the rejections have been rewritten to address these limitations.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

PADMASHRI PONNALURI
PRIMARY EXAMINER

05 May 2005